Bioorg. Med. Chem. 11 (2003) 811

A Biaryl Peptide Crosslink in a MetJ Peptide Model Confers Cooperative, Nonspecific Binding to DNA That Ablates Both Repressor Binding and In Vitro Transcription

Joshua C. Yoburn,[a] Sipra Deb,[b] Iain W. Manfield,[b] Peter G. Stockley[b] and David L. Van Vranken[a,*]

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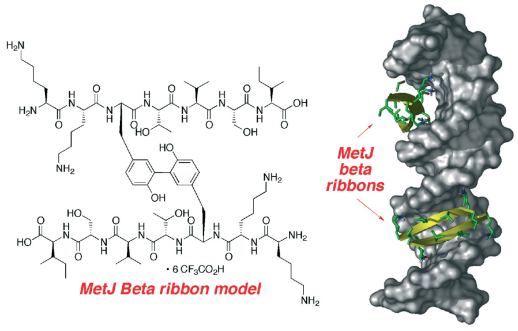
[b]*Astbury Centre for Structural Molecular Biology, School of Biochemistry and Molecular Biology, University of Leeds, Leeds, LS2 9JT, UK*

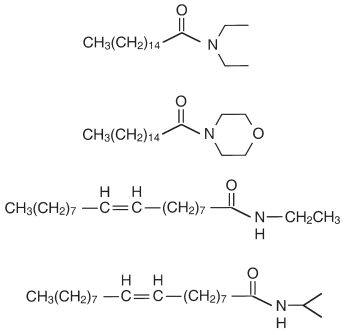


Bioorg. Med. Chem. 11 (2003) 817

N-Morpholino- and *N*-Diethyl-analogues of Palmitoylethanolamide Increase the Sensitivity of Transfected Human Vanilloid Receptors to Activation by Anandamide Without Affecting Fatty Acid Amidohydrolase Activity

Séverine Vandevoorde,[a] Didier M. Lambert,[a] Darren Smart,[b] Kent-Olov Jonsson[c] and Christopher J. Fowler[c]

[a]*Unité de Chimie pharmaceutique et de Radiopharmacie, Université catholique de Louvain, Avenue Mounier, 73, UCL-CMFA 73.40, B-1200 Brussels, Belgium*
[b]*Neurology CEDD, GlaxoSmithKline, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK*
[c]*Department of Pharmacology and Clinical Neuroscience, Umeå University, SE-901 87 Umeå, Sweden*

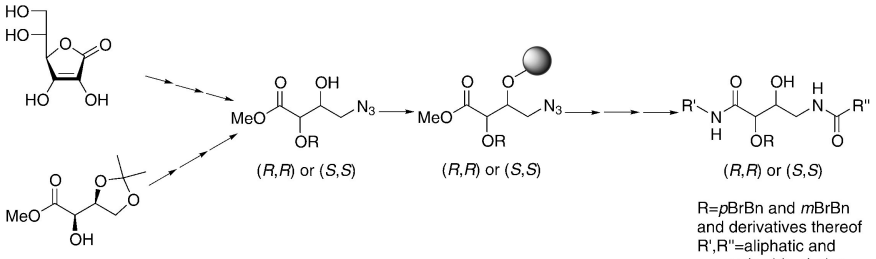


Bioorg. Med. Chem. 11 (2003) 827

Solid-Phase Library Synthesis of Reversed-Statine Type Inhibitors of the Malarial Aspartyl Proteases Plasmepsin I and II

Anders Dahlgren,[a] Ingemar Kvarnström,[a] Lotta Vrang,[b] Elizabeth Hamelink,[b] Anders Hallberg,[c] Åsa Rosenquist[a,b] and Bertil Samuelsson[b,d]

[a]*Department of Chemistry, Linköping University, S-581 83 Linköping, Sweden*
[b]*Medivir AB, Lunastigen 7, S-141 44 Huddinge, Sweden*
[c]*Department of Organic Pharmaceutical Chemistry, BMC, Uppsala University, Box 596, S-751 24 Uppsala, Sweden*
[d]*Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden*



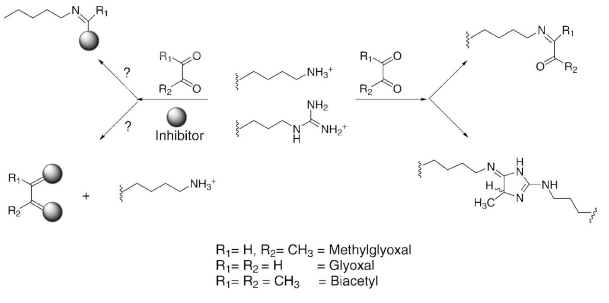
Bioorg. Med. Chem. 11 (2003) 843

New Insights Into Protein Crosslinking Via the Maillard Reaction: Structural Requirements, the Effect on Enzyme Function, and Predicted Efficacy of Crosslinking Inhibitors as Anti-ageing Therapeutics

Antonia G. Miller, Susie J. Meade and Juliet A. Gerrard

Department of Plant and Microbial Sciences, University of Canterbury, Private Bag 4800, Christchurch, New Zealand

Reported herein is an investigation of the precise structural components that are required for crosslinking of model proteins by the α-dicarbonyl compounds methylglyoxal, glyoxal and biacetyl. The effect of crosslinking on protein function is also examined. Finally, two purported Maillard reaction inhibitors have been studied in order to determine their efficacy as inhibitors of crosslinking caused by the Maillard reaction and to probe the purported causal relationship between protein crosslinking and loss of function.



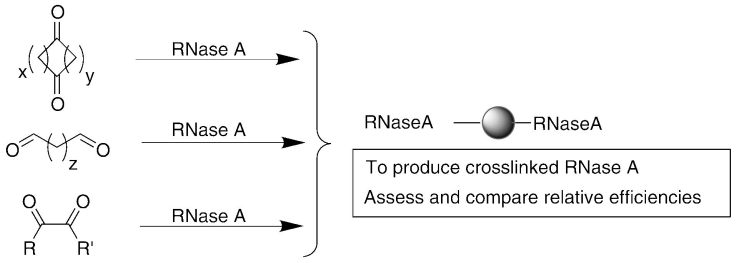
Bioorg. Med. Chem. 11 (2003) 853

The Role of Dicarbonyl Compounds in Non-enzymatic Crosslinking: A Structure–Activity Study

Susie J. Meade, Antonia G. Miller and Juliet A. Gerrard

Department of Plant and Microbial Sciences, University of Canterbury, Private Bag 4800, Christchurch, New Zealand

Reported herein is an investigation of the effect of structure of a variety of dicarbonyl compounds on the efficiency of crosslinking for the model protein RNase A.

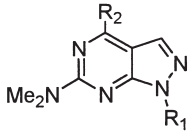


Bioorg. Med. Chem. 11 (2003) 863

6-Dimethylamino 1H-Pyrazolo[3,4-*d*]pyrimidine Derivatives as New Inhibitors of Inflammatory Mediators in Intact Cells

José M. Quintela,[a] Carlos Peinador,[a] Liliana González,[a] Isabel Devesa,[b] M. Luisa Ferrándiz,[b] Maria J. Alcaraz[b] and Ricardo Riguera[c,*]

[a]*Departamento de Química Fundamental e Industrial, Facultad de Ciencias, Universidad de La Coruña, La Coruña 15071, Spain*
[b]*Departamento de Farmacologia, Facultad de Farmacia, Universidad de Valencia 46100 Burjasot, Valencia, Spain*
[c]*Departamento de Química Orgánica, e Instituto de Acuicultura, Universidad de Santiago, Santiago de Compostela 15706, Spain*



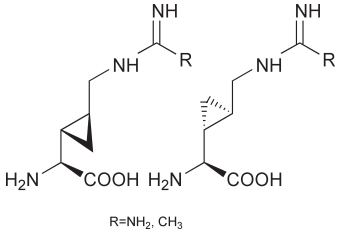
The synthesis and effect of pyrazolo[3,4-*d*]pyrimidines on murine macrophages and human neutrophils are described. Several compounds are potent PGE_2 inhibitors.

Bioorg. Med. Chem. 11 (2003) 869

Synthesis and Evaluation of *trans* 3,4-Cyclopropyl L-Arginine Analogues as Isoform Selective Inhibitors of Nitric Oxide Synthase

Dan Fishlock,[a] Basil Perdicakis,[b] Heather J. Montgomery,[a] J. Guy Guillemette,[a] Eric Jervis[b] and Gilles A. Lajoie[a,*]

[a]*Department of Chemistry, University of Waterloo, Waterloo, Ontario N2L 3G1, Canada*
[b]*Department of Chemical Engineering, University of Waterloo, Waterloo, Ontario N2L 3G1, Canada*



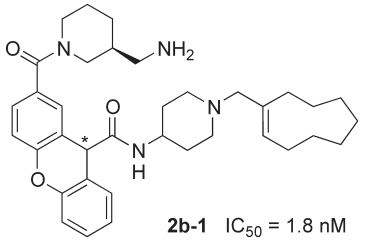
Bioorg. Med. Chem. 11 (2003) 875

Structure–activity Relationships of Xanthene Carboxamides, Novel CCR1 Receptor Antagonists

Akira Naya,* Makoto Ishikawa, Kenji Matsuda, Kenji Ohwaki, Toshihiko Saeki, Kazuhito Noguchi and Norikazu Ohtake

Banyu Tsukuba Research Institute, Okubo-3, Tsukuba 300–2611, Ibaraki, Japan

A xanthene carboxamide (**2b-1**) was discovered as a CCR1 receptor antagonist.

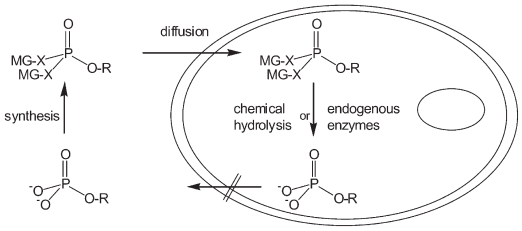


Bioorg. Med. Chem. 11 (2003) 885

Prodrugs of Biologically Active Phosphate Esters

Carsten Schultz*

European Molecular Biology Laboratory, Meyerhofstr. 1, 69117 Heidelberg, Germany



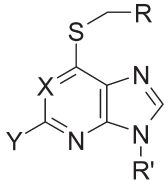
Bioorg. Med. Chem. 11 (2003) 899

Inhibition of Nucleoside Transport By New Analogues of Nitrobenzylthioinosine

Paymaneh Y. F. Deghati, Alice Borghini, Adrianus M. C. H. van den Nieuwendijk, Miriam Dissen-de Groote and Adriaan P. IJzerman

Leiden/Amsterdam Center for Drug Research, Division of Medicinal Chemistry, University of Leiden, PO Box 9502, 2300RA Leiden, The Netherlands

Derivatives of the general structure shown here were synthesized and tested as inhibitors of the human nucleoside transport protein as present on erythrocyte membranes. Several compounds showed nanomolar affinity.

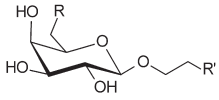


Bioorg. Med. Chem. 11 (2003) 909

Synthesis and Anti-tumor-promoting Activity of Glycoglycerolipid Analogues Lacking the Glycerol Backbone

Diego Colombo,[a] Fiamma Ronchetti,[a] Antonio Scala,[a] Lucio Toma,[b] Harukuni Tokuda[c] and Hoyoku Nishino[c]

[a]*Dipartimento di Chimica, Biochimica e Biotecnologie per la Medicina, Università di Milano, Via Saldini 50, 20133 Milan, Italy*
[b]*Dipartimento di Chimica Organica, Università di Pavia, Via Taramelli 10, 27100 Pavia, Italy*
[c]*Department of Biochemistry, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-0841, Japan*



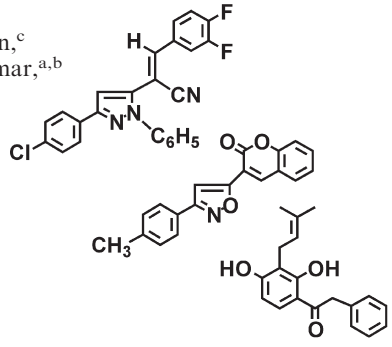
Compounds **2a**–**c** and **4** were prepared and their in vitro anti-tumor-promoting effect on Epstein–Barr virus early antigen (EBV-EA) activation promoted by the tumor promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA) was studied.

2a: R=R'=OH
2b: R=OH, R'=$OCO(CH_2)_4CH_3$
2c: R=$OCO(CH_2)_4CH_3$, R'=OH
4 : R=OH, R'=$(CH_2)_6CH_3$

Bioorg. Med. Chem. 11 (2003) 913

Synthesis, Characterization and In Vitro Anti-invasive Activity Screening of Polyphenolic and Heterocyclic Compounds

Virinder S. Parmar,[a,b,c,*] Nawal K. Sharma,[a,b] Mofazzal Husain,[a] Arthur C. Watterson,[c] Jayant Kumar,[c] Lynne A. Samuelson,[c] Ashok L. Cholli,[c] Ashok K. Prasad,[a] Ajay Kumar,[a,b] Sanjay Malhotra,[a] Naresh Kumar,[a] Amitabh Jha,[a] Amarjit Singh,[a] Ishwar Singh,[a] Himanshu,[a,b] Archana Vats,[a] Najam A. Shakil,[a,c] Smriti Trikha,[a] Shubasish Mukherjee,[a,b] Sunil K. Sharma,[a,c] Sanjay K. Singh,[a,b] Ajay Kumar,[a,d] Hriday N. Jha,[d] Carl E. Olsen,[e] Christophe P. Stove,[f] Marc E. Bracke[f] and Marc M. Mareel[f,*]



In search of anti-invasive treatments, 95 compounds of different classes have been screened in an assay for invasion consisting of organotypic confronting cultures of invasive human MCF-7/6 mammary carcinoma cells with embryonic chick heart fragments. Three compounds were found active against MCF-7/6 cells in the chick heart invasion assay at 1 μM concentration.

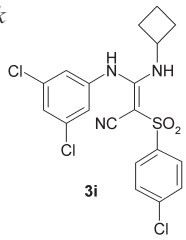
Bioorg. Med. Chem. 11 (2003) 931

Synthesis and Biological Activity of 3,3-Diamino-sulfonylacrylonitriles as Novel Inhibitors of Glucose Induced Insulin Secretion from Beta Cells

Tina M. Tagmose, Florencio Zaragoza, Harrie C. M. Boonen, Anne Worsaae, John P. Mogensen, Flemming E. Nielsen, Anette Frost Jensen and John Bondo Hansen*

Health Care Discovery and Development Novo Nordisk A/S, Novo Nordisk Park, DK-2760, Måløv, Denmark

Novel 3,3-diamino-sulfonylacrylonitriles, for example **3i**, have been synthesised and identified as potent inhibitors of glucose stimulated insulin secretion from beta cell lines and rat pancreatic islets with minimal effects on vascular smooth muscle.

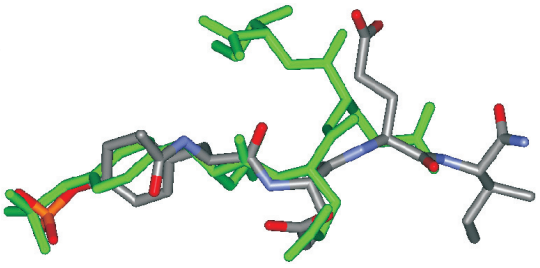


Bioorg. Med. Chem. 11 (2003) 941

Role of Solution Conformation and Flexibility of Short Peptide Ligands that Bind to the p56^{lck} SH2 Domain

Frank J. Dekker,[a] Nico J. de Mol,[a,*] Patrick Bultinck,[b] Johan Kemmink,[a] Hans W. Hilbers[a] and Rob M. J. Liskamp[a]

[a]*Department of Medicinal Chemistry, Utrecht Institute of Pharmaceutical Sciences, Faculty Pharmaceutical Sciences, Utrecht University, PO Box 80082, 3508TB Utrecht, The Netherlands*
[b]*Department of Inorganic and Physical Chemistry, Ghent University, Krijgslaan 281(S-3), B-9000 Gent, Belgium*



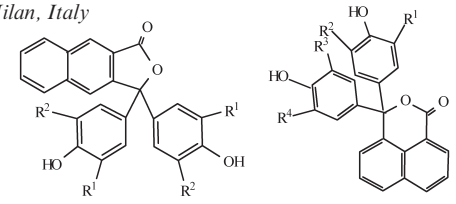
Bioorg. Med. Chem. 11 (2003) 951

ortho-Halogen Naphthaleins as Specific Inhibitors of *Lactobacillus casei* Thymidylate Synthase. Conformational Properties and Biological Activity

Stefano Ghelli,[a] Marcella Rinaldi,[b] Daniela Barlocco,[c] Arianna Gelain,[c] Piergiorgio Pecorari,[b] Donatella Tondi,[b] Giulio Rastelli[b] and Maria Paola Costi[b,*]

[a]*Dipartimento di Chimica, Universita' degli Studi di Modena e Reggio Emilia, Via Campi 183 41100, Modena, Italy*
[b]*Dipartimento di Scienze Farmaceutiche, Universita' degli Studi di Modena e Reggio Emilia, Via Campi 183, 41100 Modena, Italy*
[c]*Istituto Chimico Farmaceutico, Università degli Studi di Milano, Viale Abruzzi 42, 20131 Milan, Italy*

With the aim of investigating the specificity of 1,8-naphthalein derivatives towards *Lactobacillus casei* thymidylate synthase with respect to human Thymidylate Synthase two series of variously substituted derivatives of 3,3-bis (4-hydroxyphenyl)-*1H,3H*-naphtho[2,3-*c*]furan-1-one and 3,3-bis(4-hydroxyphenyl)-*1H,3H*-naphtho[1,8-*c,d*]pyran-1-one were synthesized. The conformational properties of the compounds were studied through ^{1}H NMR and quantum chemical calculations.



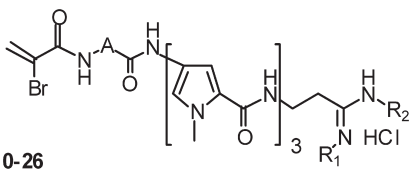
Bioorg. Med. Chem. 11 (2003) 965

Synthesis and Growth Inhibition Activity of α-Bromoacrylic Heterocyclic and Benzoheterocyclic Derivatives of Distamycin a Modified on the Amidino Moiety

Pier Giovanni Baraldi,[a,*] Italo Beria,[b] Paolo Cozzi,[b] Nicoletta Bianchi,[c] Roberto Gambari[c] and Romeo Romagnoli[c]

[a]*Dipartimento di Scienze Farmaceutiche, Università di Ferrara, 44100 Ferrara, Italy*
[b]*Pharmacia, Global Chemistry, Discovery Research Oncology, Nerviano, Milan, Italy*
[c]*Dipartimento di Biochimica e Biologia Molecolare, Università di Ferrara, 44100 Ferrara, Italy*

The design, synthesis and in vitro activities of novel α-bromoacryloyl pyrazole, imidazole and benzoheterocyclic derivatives of distamycin A, in which the amidino moiety has been replaced by moieties of different physico-chemical features are described.



10-26
A=heterocycle or benzoheterocycle
R_1= R_2 or R_1=R_2, where R_1 and R_2 are H, CH_3 and CN

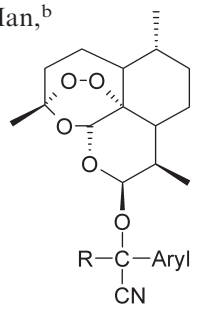
Bioorg. Med. Chem. 11 (2003) 977

Synthesis and Cytotoxicity of Dihydroartemisinin Ethers Containing Cyanoarylmethyl Group

Ying Li,[a,*] Jin-Ming Wu,[a] Feng Shan,[a] Guang-Shao Wu,[a] Jian Ding,[b] Dong Xiao,[b] Jia-Xian Han,[b] Ghanem Atassi,[c] Stéphane Leonce,[c] Daniel-Henri Caignard[d] and Pierre Renard[d]

[a]*Department of Synthetic Chemistry, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China*
[b]*Department of pharmacology, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China*
[c]*Institut de Recherche Servier, Suresnes, France*
[d]*ADIR ET COMPAGNIE, Courbevoie, France*

A new type of ether of dihydroartemisinin containing cyano and aryl groups was prepared and tested for cytotoxicity to A549, P388, L1210 and HT29 cells using the MTT assay. Their structure–activity relationship was discussed.

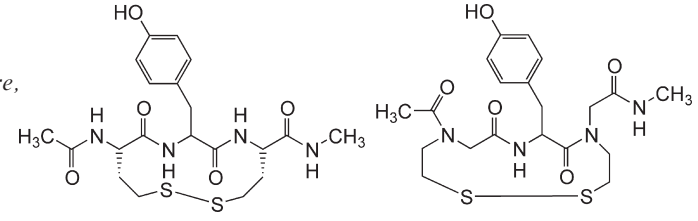


Bioorg. Med. Chem. 11 (2003) 985

A Frame Shifted Disulfide Bridged Analogue of Angiotensin II

Boris Schmidt,[a,*] Christian Kühn,[b] Dennis K. Ehlert,[b] Gunnar Lindeberg,[c] Susanna Lindman,[c] Anders Karlén[c] and Anders Hallberg[c]

[a]*TU Darmstadt, Institut for Organic Chemistry, Petersenstr. 22, D-64287 Darmstadt, Germany*
[b]*Institut für Organische Chemie der Universität Hannover, Schneiderberg 1b, D-30167 Hannover, Germany*
[c]*Departments of Organic Pharmaceutical Chemistry, Medical Biochemistry and Microbiology, Biomedical Centre, Uppsala University, Box 574, SE-751 23 Uppsala, Sweden*

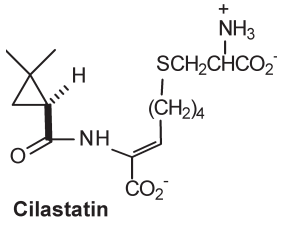


Bioorg. Med. Chem. 11 (2003) 991

A Substrate Variant as a High-Affinity, Reversible Inhibitor: Insight from the X-ray Structure of Cilastatin Bound to Membrane Dipeptidase

Timothy P. Smyth,[a,*] J. Gerard Wall[a] and Yasushi Nitanai[b]

[a]*Department of Chemical and Environmental Sciences, Univeristy of Limerick, National Technological Park, County Limerick, Ireland*
[b]*Suntory Institute for Biomedical Research, Shimamoto-cho, Mishima-gun, Osaka 618, Japan*



Cilastatin

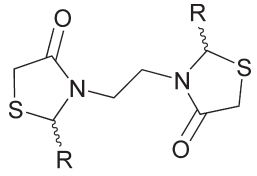
Bioorg. Med. Chem. 11 (2003) 999

Chiral 3,3′-(1,2-Ethanediyl)-bis[2-(3,4-dimethoxyphenyl)-4-thiazolidinones] with Anti-Inflammatory Activity. Part 11: Evaluation of COX-2 Selectivity and Modelling

M. G. Vigorita,[a,*] R. Ottanà,[a] F. Monforte,[a] R. Maccari,[a] M. T. Monforte,[b] A. Trovato,[b] M. F. Taviano,[b] N. Miceli,[b] G. De Luca,[c] S. Alcaro[d] and F. Ortuso[d]

[a]*Dipartimento Farmaco-chimico, Facoltà di Farmacia Università di Messina, Viale SS. Annunziata, 98168 Messina, Italy*
[b]*Dipartmento Farmaco-biologico, Facoltà di Farmacia Università di Messina, Viale SS. Annunziata, 98168 Messina, Italy*
[c]*Istituto di Scienze Biochimiche e Biochimica Clinica, Facoltà di Medicina e Chirurgia Università di Messina, Policlinico Universitario 'G. Martino', V. Cons. Valeria, 98124 Messina, Italy*
[d]*Dipartimento di Scienze Farmacobiologiche, Università di Catanzaro 'Magna Græcia', Roccelletta di Borgia, Catanzaro, Italy*

The titled bisthiazolidinones were found to be diastereo- and enantioselective preferential COX-2 inhibitors.



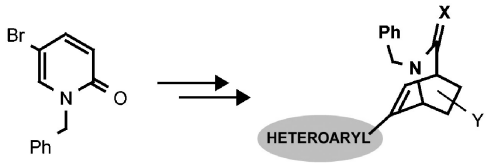
R = 3,4-$(OMe)_2$-C_6H_3
rac. 2R,2'R/2S,2'S (**a**)
2R,2'S-*meso* (**b**)

Bioorg. Med. Chem. 11 (2003) 1007

Ibogaine Analogues. Synthesis and Preliminary Pharmacological Evaluation of 7-Heteroaryl-2-azabicyclo[2.2.2]oct-7-enes

Daniele Passarella,[a,*] Raffaele Favia,[a] Alessandra Giardini,[a] Giordano Lesma,[a] Marisa Martinelli,[a] Alessandra Silvani,[a] Bruno Danieli,[a] Simon M. N. Efange[b] and Deborah C. Mash[c]

[a]*Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milan, Via Venezian 21, 20133 Milano, Italy*
[b]*Departments of Radiology, University of Minnesota, MN 55455, USA*
[c]*Department of Neurology and Molecular & Cellular Pharmacology, University of Miami School of Medicine, FL 33136, USA*



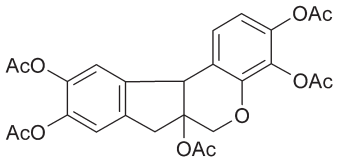
Bioorg. Med. Chem. 11 (2003) 1015

Mechanism of Biochemical Action of Substituted 4-Methylbenzopyran-2-ones. Part 10: Identification of Inhibitors for the Liver Microsomal Acetoxycoumarin: Protein Transacetylase

Hanumantharao G. Raj,[a] Ishwar Singh,[b] Ekta Kohli,[a] Ranju Kumari,[a] Garima Gupta,[a] Yogesh K. Tyagi,[a] Ajit Kumar,[a] Ashok K. Prasad,[b] Narendra K. Kaushik,[b] Carl E. Olsen,[c] Arthur C. Watterson[d] and Virinder S. Parmar[b,d,*]

[a]*Department of Biochemistry, V P Chest Institute, University of Delhi, Delhi-110 007, India*
[b]*Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110 007, India*
[c]*Chemistry Department, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark*
[d]*Institute of Nano Science Engineering and Technology, Department of Chemistry, University of Massachusetts, One University Avenue, Lowell, MA 01854, USA*

Catechin pentaacetate was found to be an effective inhibitor for acetoxycoumarin: protein transacetylase (TAase), so also were 7-acetoxy-3,4-dihydro-2,2-dimethylbenzopyran and hematoxylin pentaacetate. These results prompt that acetoxybenzopyran derivatives merit as the inhibitors of TAase.



Hematoxylin pentaacetate

Bioorg. Med. Chem. 11 (2003) 1021

Water Soluble Prodrugs of the Antitumor Agent 3-[(3-Amino-4-methoxy)phenyl]-2-(3,4,5-trimethoxyphenyl)cyclopent-2-ene-1-one

Nguyen-Hai Nam,[a,*] Yong Kim,[a] Young-Jae You,[a] Dong-Ho Hong,[a,b] Hwan-Mook Kim[b] and Byung-Zun Ahn[a,*]

[a]*College of Pharmacy, Chungnam National University, Taejon 305-764, South Korea*
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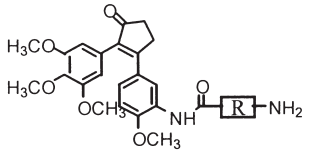
A series of amino acid and phosphate prodrugs of the tittle antitumor agent was synthesized and evaluated. Most prodrugs showed increase antitumor activity.



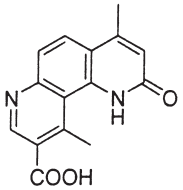
Bioorg. Med. Chem. 11 (2003) 1031

Synthesis and Bioactivity of 4,10-Dimethyl-pyridino[2,3-*h*]quinolin-2(1*H*)-one-9-carboxylic Acid and Its Esters

Qian Zhang,[a] Ying Chen,[a] Yun Qing Zheng,[a] Peng Xia,[a,*] Yi Xia,[b] Zheng Yu Yang,[b] Kenneth F. Bastow,[b] Susan L. Morris-Natschke[b] and Kuo-Hsiung Lee[b,*]

[a]*Department of Medicinal Chemistry, School of Pharmacy, Fudan University, Shanghai 200032, China*
[b]*Natural Products Laboratory, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599, USA*

4,10-Dimethyl-pyridino[2,3-*h*]quinolin-2(1*H*)-one-9-carboxylic acid (**1**) was synthesized by a new approach via the key intermediate 7-[1-aza-2-(dimethylamino)vinyl]-4-methylquinolin-2(1*H*)-one (**4**). The 9-carboxyl (1s)-endo-(−)-borneol ester (**9**) showed marginal cytotoxic activity in CAK1-1, HOS, KB, and HCT-8 cells.



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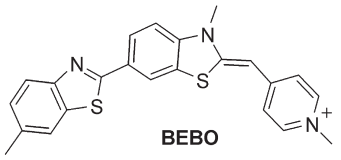
Bioorg. Med. Chem. 11 (2003) 1035

Synthesis and DNA Binding Studies of a New Asymmetric Cyanine Dye Binding in the Minor Groove of $[poly(dA\text{-}dT)]_2$

H. Jonas Karlsson, Per Lincoln and Gunnar Westman*

Department of Chemistry and Bioscience, Chalmers University of Technology, Kemivägen 10, S-41296 Göteborg, Sweden



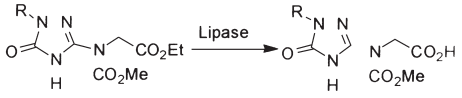
Bioorg. Med. Chem. 11 (2003) 1041

Purification and Characterization of an Alkaline Lipase from a Newly Isolated *Pseudomonas mendocina* PK-12CS and Chemoselective Hydrolysis of Fatty Acid Ester

Umesh K. Jinwal,[a] Uma Roy,[b] Abhijit R. Chowdhury,[c] A. P. Bhaduri[c] and P. K. Roy[a,*]

[a]*Division of Fermentation Technology, Central Drug Research Institute, Lucknow-226 001, India*
[b]*Division of Biochemistry, Central Drug Research Institute, Lucknow-226 001, India*
[c]*Division of Chemistry, Central Drug Research Institute, Lucknow-226 001, India*

Lipase isolated from a soil isolate *P. mendocina* chemoselectively hydrolyzed the fatty ester group in presence of carbamate in 5-amino-2,4-dihydro-3H-1,2,4-triazole-3-ones.



Bioorg. Med. Chem. 11 (2003) 1047

New Fluorinated Derivatives as Esterase Inhibitors. Synthesis, Hydration and Crossed Specificity Studies

Carmen Quero,[a] Gloria Rosell,[b] Oscar Jiménez,[a] Sergio Rodriguez,[a] M. Pilar Bosch[a] and Angel Guerrero[a,*]

[a]*Department of Biological Organic Chemistry, Institute of Chemistry and Environmental Research (CSIC), Jordi Girona 18-26, 08034 Barcelona, Spain*
[b]*Department of Pharmacology and Therapeutic Chemistry, Unity Associated to CSIC, Faculty of Pharmacy, University of Barcelona, Avda. Diagonal, s/n. 08028 Barcelona, Spain*

Trifluoromethyl and difluoromethyl ketones and difluoroaldehydes have been prepared and tested as inhibitors of esterases, the pheromone catabolism enzymes, of two economically important pests.

RCF_2COR' R=alkyl, alkenyl, R'=alkyl, aryl
RCF_2CHO R=alkyl, alkenyl
$RCOCF_3$ R=methylthioalkyl, alkenyl, alkadienyl

Bioorg. Med. Chem. 11 (2003) 1057

Curcumin Differentially Modulates mRNA Profiles in Jurkat T and Human Peripheral Blood Mononuclear Cells

Jürg Gertsch, Martin Güttinger, Jörg Heilmann* and Otto Sticher

Swiss Federal Institute of Technology Zurich, Institute of Pharmaceutical Sciences, Winterthurerstrasse 190, 8057 Zürich, Switzerland

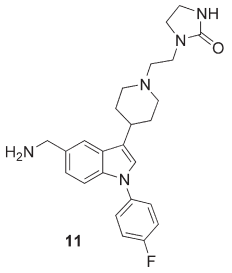
The effects of curcumin on gene expression in T Jurkat $CD4^+$ and human peripheral blood mononuclear cells (PBMCs) were characterized with reverse transcription real-time PCR. The relative quantification of the mRNA levels of β-actin, GAP-DH, GM-CSF, IFN-γ, IL-2, IL-6, I-κBα, p65, NF-Atc, cyclin D1, and iNOS showed that curcumin differentially modulates the expression profile of Th1 cells and PBMCs at low concentrations.

Bioorg. Med. Chem. 11 (2003) 1065

Synthesis and Structure–Affinity Relationship Investigations of 5-Aminomethyl and 5-Carbamoyl Analogues of the Antipsychotic Sertindole. A New Class of Selective α_1 Adrenoceptor Antagonists

Thomas Balle,[a,b] Jens Perregaard,[a] Anna K. Larsen,[c] Martha Teresa Ramirez,[c] Karina Krøjer Søby,[c] Tommy Liljefors[b] and Kim Andersen[a,*]

[a]*Medicinal Chemistry Research, H. Lundbeck A/S, 9 Ottiliavej, DK-2500 Valby, Denmark*
[b]*Department of Medicinal Chemistry, The Royal Danish School of Pharmacy, 2 Universitetsparken, DK- 2100 Copenhagen, Denmark*
[c]*Biological Research, H. Lundbeck A/S, 9 Ottiliavej, DK-2500 Valby, Denmark*



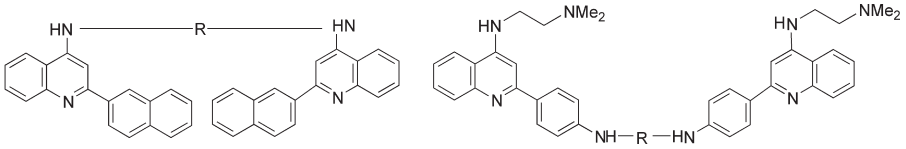
Ki (nM) = 0.18/1.1/0.69 $\alpha_{1a}/\alpha_{1b}/\alpha_{1d}$
Selectivity > 44 X ($D_{2\text{-}4}$, 5-$HT_{1A/B}$, 5-$HT_{2A/C}$)

Bioorg. Med. Chem. 11 (2003) 1079

Bis-4-aminoquinolines Novel Triple-Helix DNA Intercalators and Antagonists of Immunostimulatory CpG-Oligodeoxynucleotides

Lucjan Strekowski,[a] Martial Say,[a] Oliwia Zegrocka,[a] Farial A. Tanious,[a] W. David Wilson,[a] Lori Manzel[b] and Donald E. Macfarlane[b]

[a]*Department of Chemistry, Georgia State University, Atlanta, GA 30303, USA*
[b]*Department of Medicine, Veterans Affairs Medical Center and University of Iowa, Iowa City, IA 52242, USA*

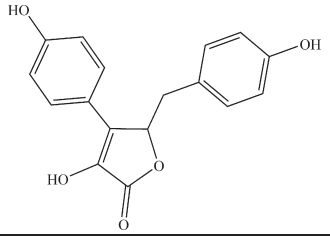


Bioorg. Med. Chem. 11 (2003) 1087

Synthesis and Antioxidant Properties of a New Lipophilic Ascorbic Acid Analogue

Philippe Cotelle,[a] Nicole Cotelle,[a] Elisabeth Teissier[b] and Hervé Vezin[a]

[a]*Laboratoire de Chimie Organique et Macromoléculaire, UPRESA CNRS 8009, Université des Sciences et Technologies de Lille, 59655 Villeneuve d'Ascq, France*
[b]*Département de recherches sur les lipoprotéines et l'athérosclérose, INSERM U325, Institut Pasteur et Faculté de Pharmacie, Université de Lille 2, 59000 Lille, France*



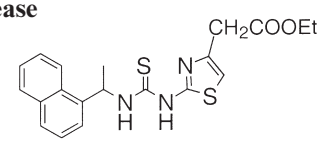
Compound **1** was prepared by an acidic dimerisation of 4-hydroxyphenylpyruvic acid and some of its antioxidant and spectroscopic properties have been measured and compared to that of ascorbic acid. Compound **1** is as good antioxidant as ascorbic acid in the DPPH test and the inhibition of hydroxyl radical and a powerful inhibitor of the Cu^{2+} or AAPH induced oxidation of human LDL. Compound **1** presents an ESR spectrum similar to ascorbyl radical but in lower concentration and a different reactivity towards nitroxide. Theoretical calculations allow us to propose the structure for the radical formed from **1**, explain its lower stability than ascorbyl radical and evaluate the lipophilicity of **1**.

Bioorg. Med. Chem. 11 (2003) 1095

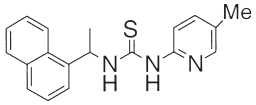
Substituted Heterocyclic Thiourea Compounds as a New Class of Anti-allergic Agents Inhibiting IgE/FcεRI Receptor Mediated Mast Cell Leukotriene Release

T. K. Venkatachalam,[a] S. Qazi,[b] P. Samuel[c] and F. M. Uckun[d,e,f]

[a]*Department of Chemistry, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[b]*Department of Bioinformatics, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[c]*Department of Pharamaceutical Sciences, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[d]*Department of Immunology, Parker Hughes Institute, 2699 Patton Road, Roseville, MN 55113, USA*
[e]*Drug Discovery Program, Parker Hughes Center for Clinical Immunology, 2848 Patton Road, Roseville, MN 55113, USA*
[f]*Drug Discovery Program, Parker Hughes Cancer Center, 2848 Patton Road, Roseville, MN 55113, USA*



(17)



(5)

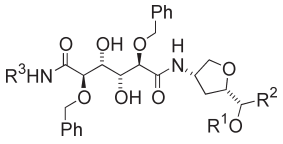
Heterocyclic thiourea compounds were synthesized as a new class of anti-allergic agents and examined for their in-vitro effects on IgE/FcεRI receptor mediated mast cell leukotriene release. Compounds **17** and **5** were identified as lead compounds with IC_{50} values of 2–5 nM.

Bioorg. Med. Chem. 11 (2003) 1107

Design and Synthesis of HIV-1 Protease Inhibitors. Novel Tetrahydrofuran P2/P2′-Groups Interacting with Asp29/30 of the HIV-1 Protease. Determination of Binding from X-ray Crystal Structure of Inhibitor Protease Complex

Karin Oscarsson,[a] Martina Lahmann,[a] Jimmy Lindberg,[b] Jussi Kangasmetsä,[c] Torsten Unge,[b] Stefan Oscarson,[a] Anders Hallberg[d] and Bertil Samuelsson[a]

[a]*Department of Organic Chemistry, Arrhenius Laboratory, Floor 6, Stockholm University, S-106 91 Stockholm, Sweden*
[b]*Department of Cell and Molecular Biology, BMC, Uppsala University, Box 596, S-751 24 Uppsala, Sweden*
[c]*Medivir AB, Lunastigen 7, S-141 44 Huddinge, Sweden*
[d]*Department of Organic Pharmacutical Chemistry, BMC, Uppsala University, Box 574, S-751 23 Uppsala, Sweden*



Bioorg. Med. Chem. 11 (2003) 1117

Modes of Antifungal Action of Alkanols against *Saccharomyces cerevisiae*

Isao Kubo,* Tomoko Fujita, Aya Kubo and Ken-ichi Fujita

Department of Environmental Science, Policy and Management, University of California, Berkeley, CA 94720-3112, USA

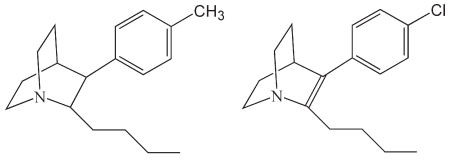
Primary aliphatic alcohols from C_6 to C_{13} were tested for their antifungal activity against *Saccharomyces cerevisiae*. Undecanol was found to be the most potent fungicide followed by decanol. The time–kill curve study showed that undecanol was fungicidal against *S. cerevisiae* at any growth stage. The primary antifungal action of amphipathic medium-chain alkanols comes mainly from their ability as nonionic surfactants to disrupt the native membrane associated function of the integral proteins.

Bioorg. Med. Chem. 11 (2003) 1123

2,3-Disubstituted Quinuclidines as a Novel Class of Dopamine Transporter Inhibitors

Sukumar Sakamuri,[a] Istvan J. Enyedy,[b,c] Wahiduz A. Zaman,[d] Srihari R. Tella,[e] Alan P. Kozikowski,[a] Judith L. Flippen-Anderson,[f] Tivadar Farkas,[g] Kenneth M. Johnson[d] and Shaomeng Wang[b,c,*]

[a]*Department of Neurology, Georgetown University Medical Center, 3900 Reservoir Rd., Washington, DC 20007, USA*
[b]*Department of Oncology, Georgetown University Medical Center, 3900 Reservoir Rd., Washington, DC 20007, USA*
[c]*Department of Neuroscience, Georgetown University Medical Center, 3900 Reservoir Rd., Washington, DC 20007, USA*
[d]*Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77555-1031, USA*
[e]*Department of Pharmacology, Georgetown University Medical Center, 3900 Reservoir Rd., Washington, DC 20007, USA*
[f]*Laboratory for the Structure of Matter, Naval Research Laboratory, 4555 Overlook Avenue, Washington, DC 20375-5341, USA*
[g]*Phenomenex, Inc., 2320 W. 205th Street, Torrance, CA 90501, USA*



Bioorg. Med. Chem. 11 (2003) 1137

Antitumor Agents 220. Antitumor-Promoting Effects of Cimigenol and Related Compounds on Epstein–Barr Virus Activation and Two-Stage Mouse Skin Carcinogenesis

Nobuko Sakurai,[a] Mutsuo Kozuka,[a] Harukuni Tokuda,[b] Yoshitaka Nobukuni,[b] Junko Takayasu,[b] Hoyoku Nishino,[b] Akiko Kusano,[c] Genjiro Kusano,[c] Masahiro Nagai,[d] Yojiro Sakurai[a] and Kuo-Hsiung Lee[a,e]

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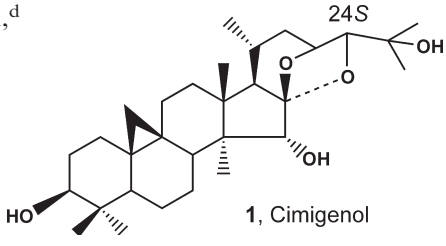
[b]*Department of Biochemistry, Kyoto Prefectural University of Medicine, Kamigyo-ku, Kyoto 602-0841, Japan*
[c]*Osaka University of Pharmaceutical Science, Nasahara, Takatsuki 569-1094, Japan*
[d]*Hoshi University, Ebara, Shinagawa-ku, Tokyo 142-8501, Japan*
[e]*Plantaceutica, Inc., 99 Alexander Drive, Research Triangle Park, NC 27709-2060, USA*



1, Cimigenol